



Tempo, sesso, genere, storia e demenza

Time, sex, gender, history, and dementia

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Outline

1. The decline of dementia: **time**

- Alzheimer's disease (AD) vs. dementia
- History: USA, Canada, and UK
- Possible opposing trends for AD and other dementias

2. Possible explanations: **sex, gender, history**

- Sex and gender factors
- Positive individual and societal changes
- Changes in smoking, diet, and lifestyle
- Changes in education and socioeconomic factors
- Changes in intelligence quotient (IQ)
- Negative individual and societal changes

3. Conclusions: hope for prevention

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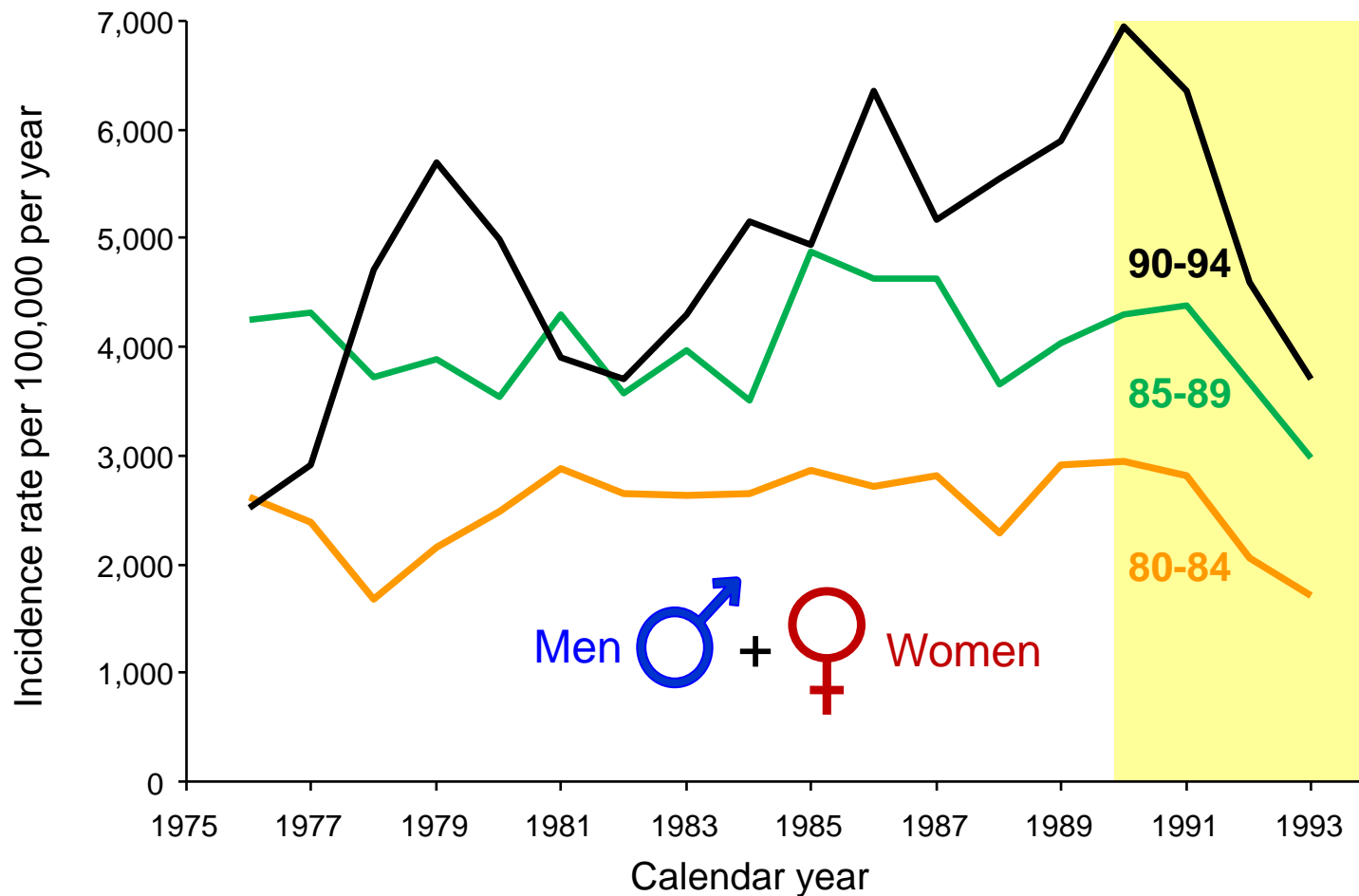
The decline of dementia

Πάντα ῥεῖ (panta rhei)

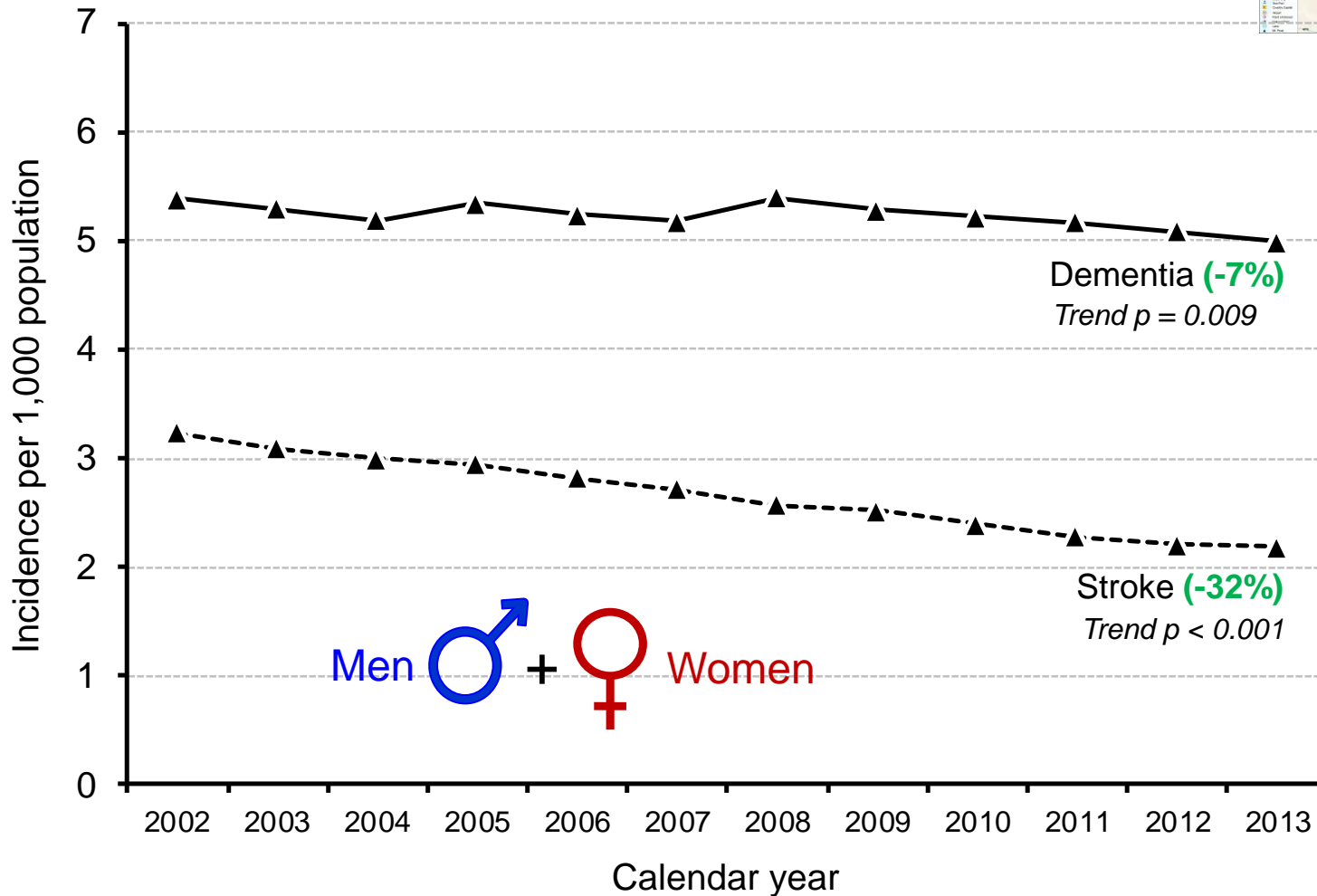
Everything flows

(Heraclitus, 535-475 BC)

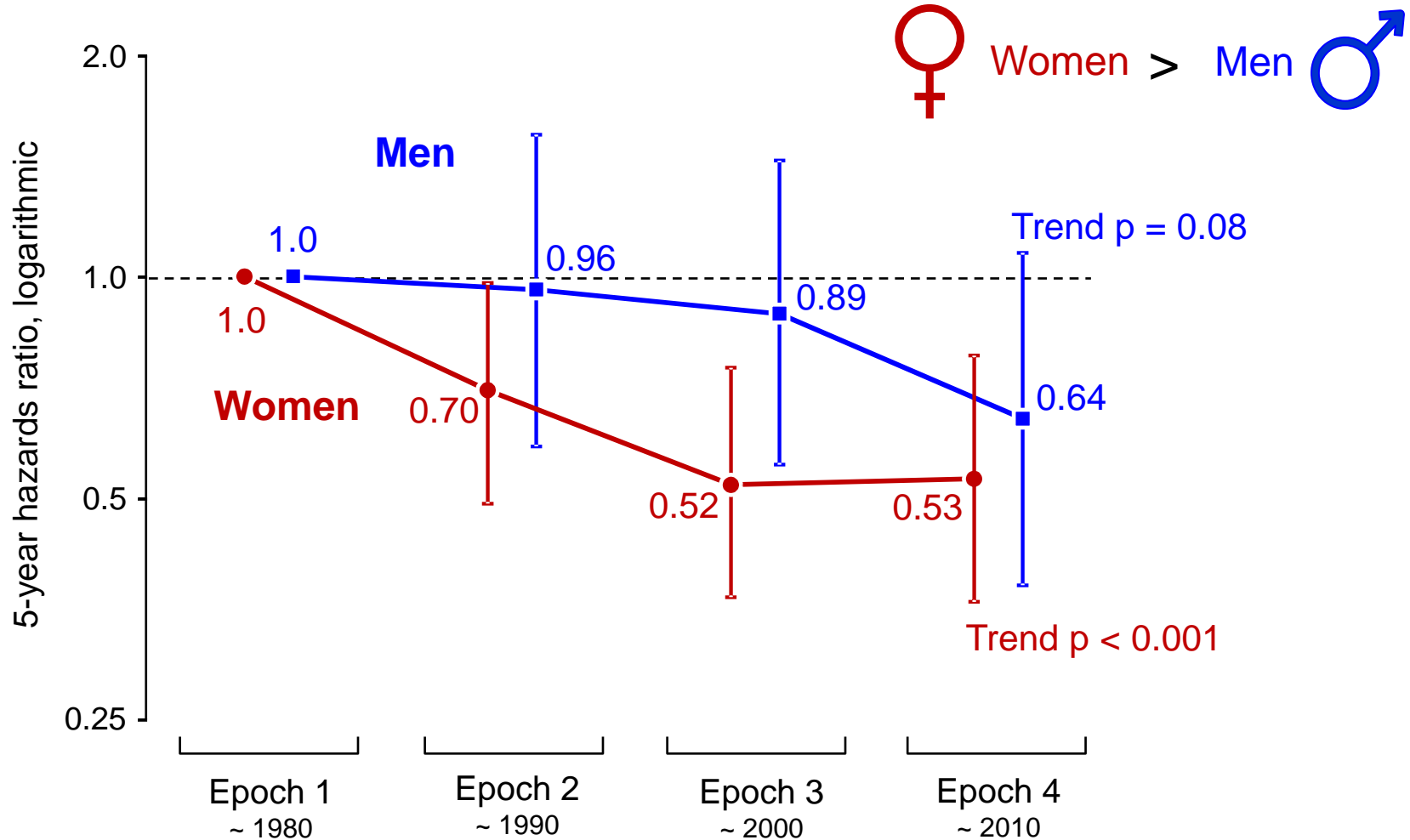
2011: Time trends for dementia Olmsted Co., Minnesota



2015: Time trends for dementia Canada





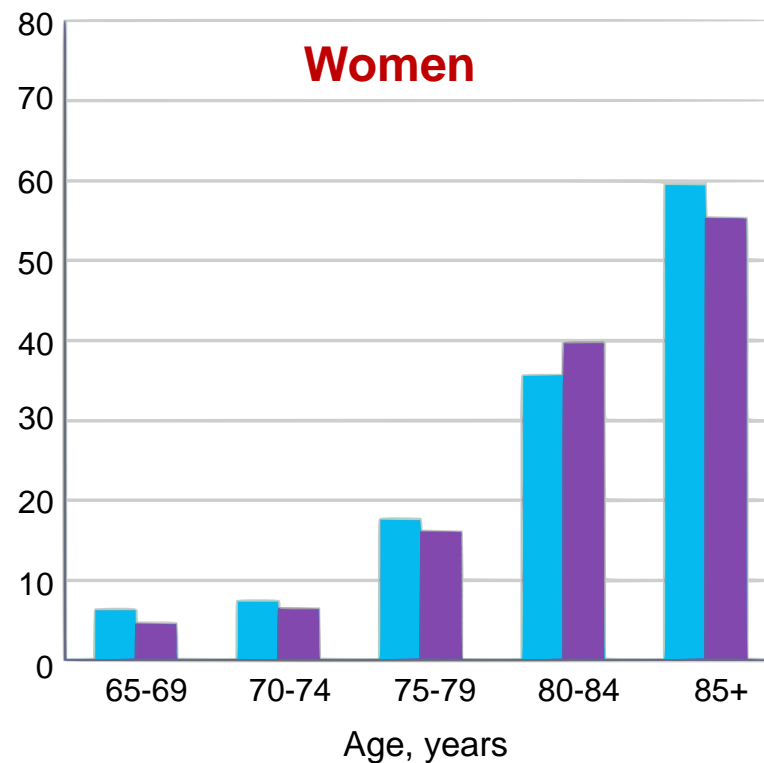
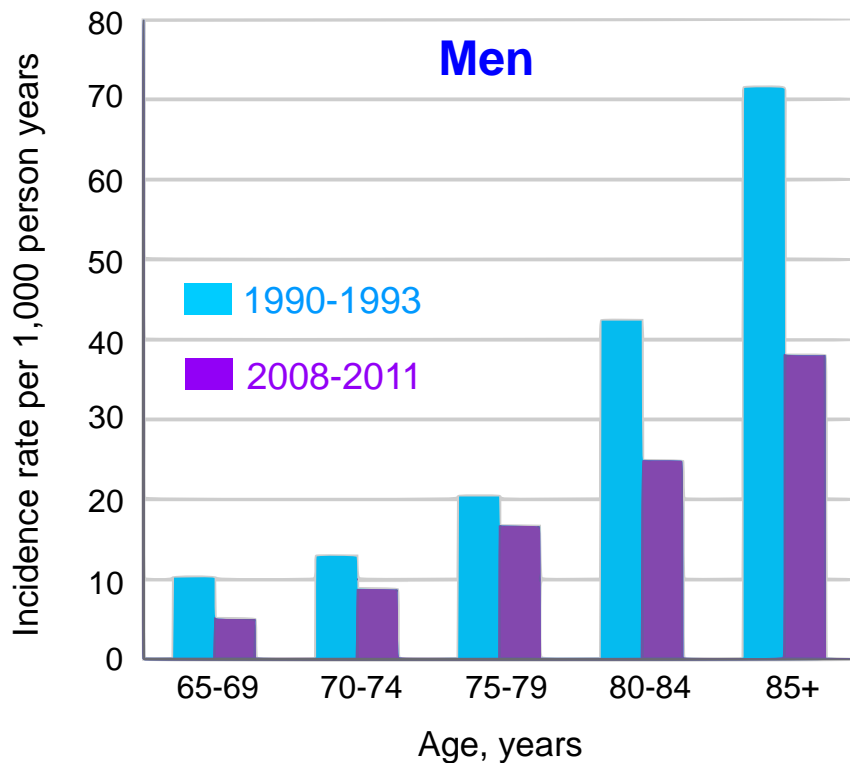
2016: Time trends for dementia Framingham, Massachusetts



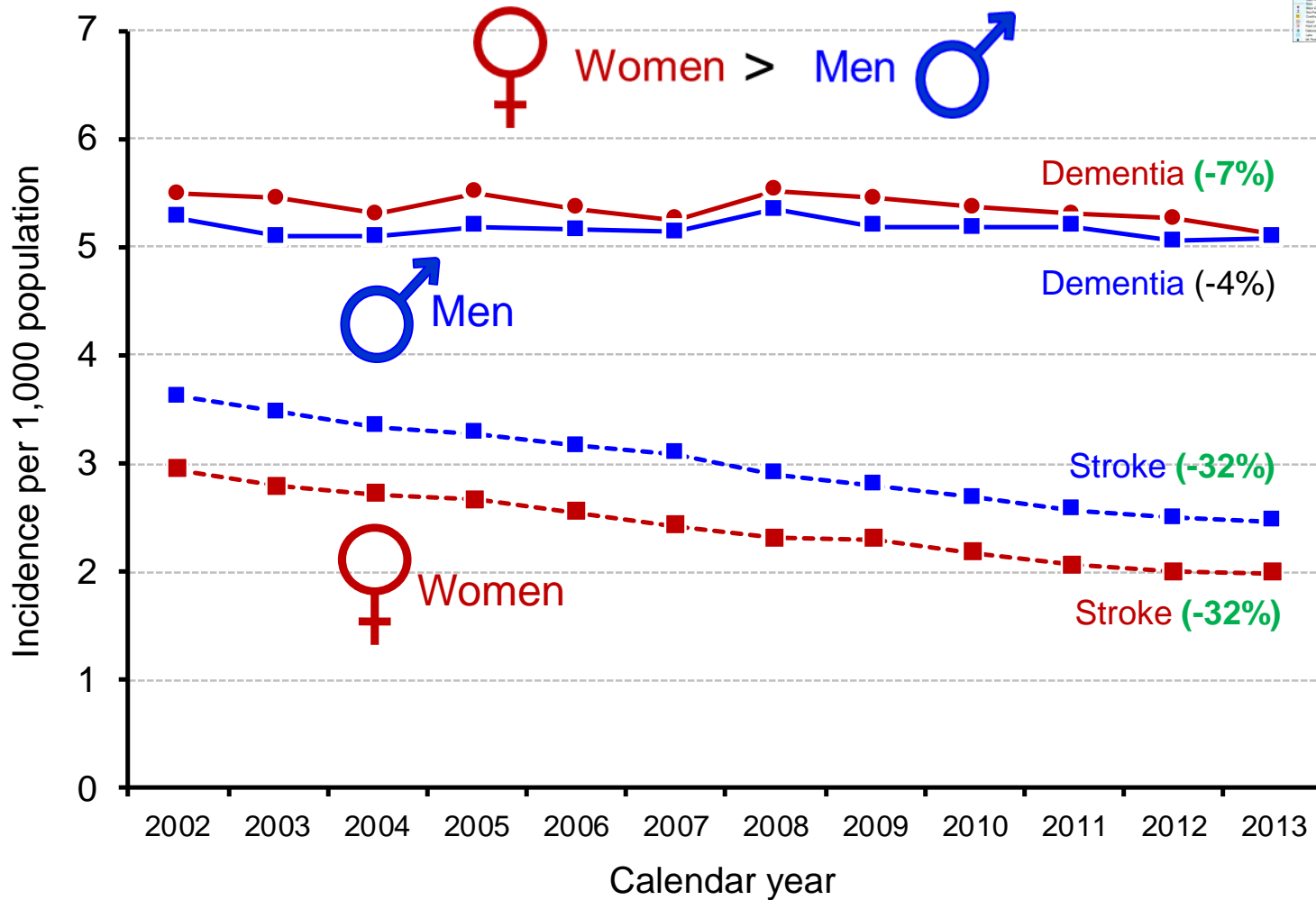
2016: Time trends for dementia United Kingdom - 3 areas



Men  >  Women



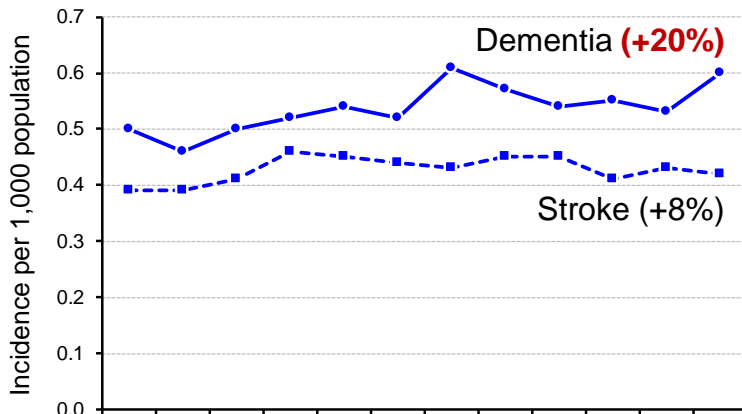
2017: Time trends for dementia Canada



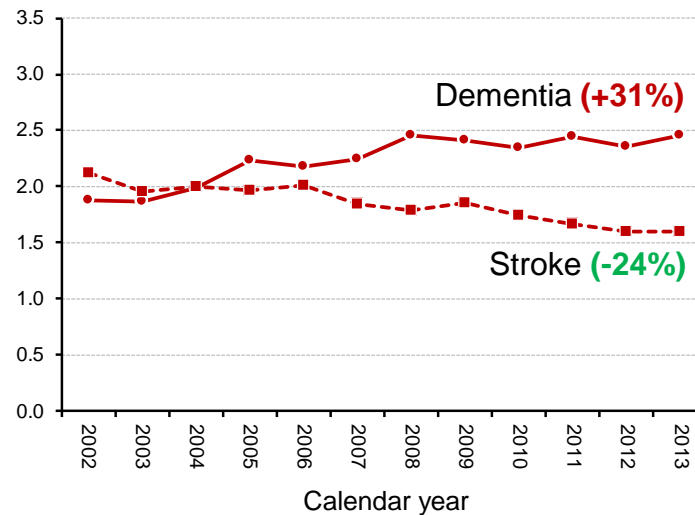
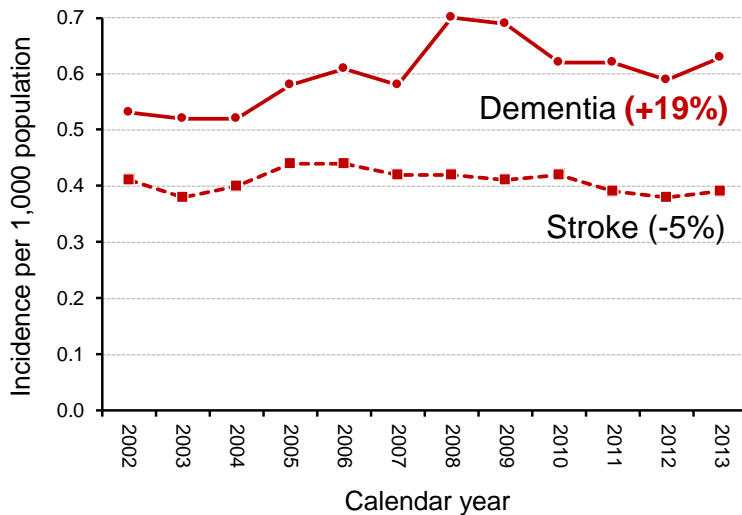
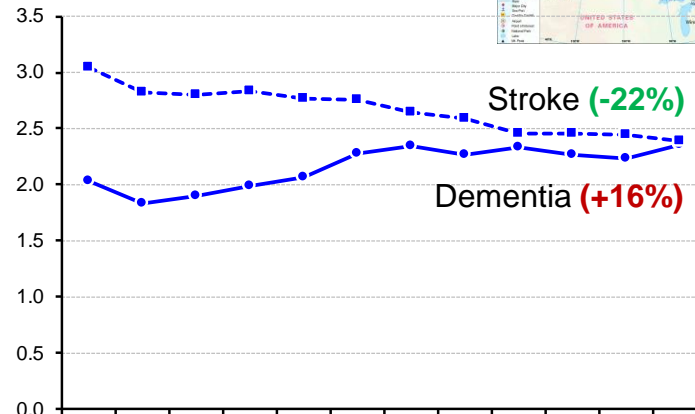
2017: Time trends for dementia Canada



Ages 20-49



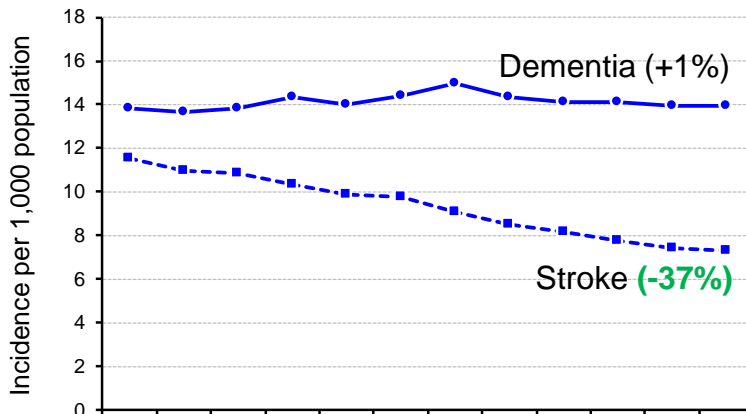
Ages 50-64



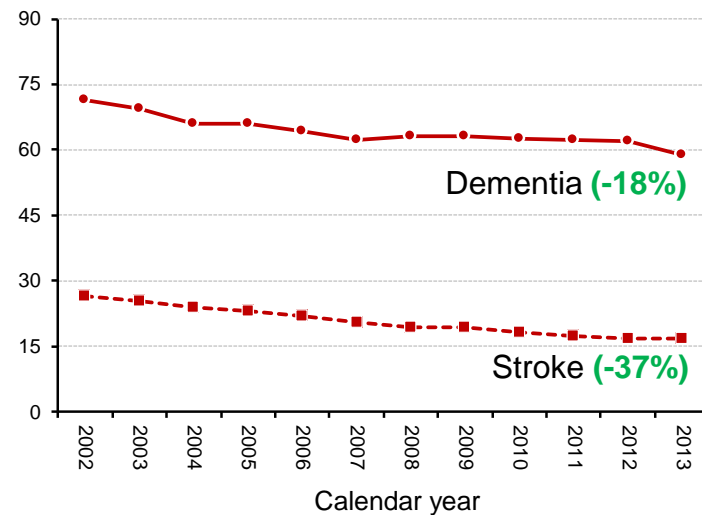
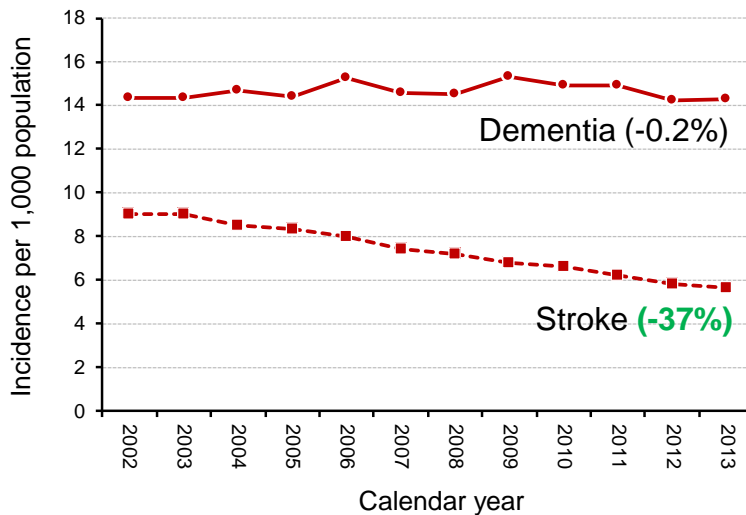
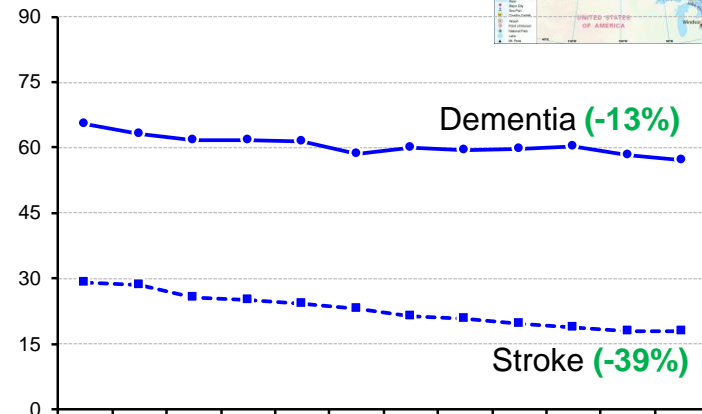
2017: Time trends for dementia Canada



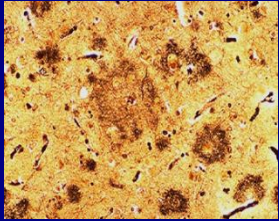
Ages 65-79



Ages 80+



Dementia vs. Alzheimer's disease



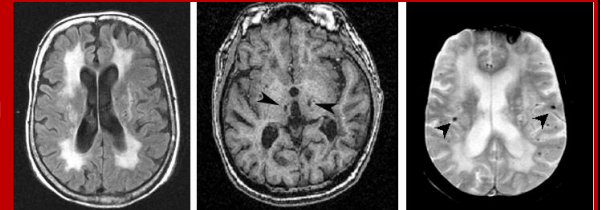
Neurodegenerative burden

Alzheimer pathology
Cortical Lewy bodies

Alzheimer's
disease

Vascular
dementia

Vascular cerebral lesion burden



Possible opposing trends

- Dementia with late onset, limited familial aggregation, and predominant neurovascular lesions is decreasing over time
- Dementia with early onset, familial aggregation, and predominant neurodegenerative lesions is increasing over time
- Late onset dementia drives the overall trend
- Supporting evidence:
 - Decline in the incidence of stroke
 - Increase in the incidence of parkinsonism
 - Increase in the incidence of amyotrophic lateral sclerosis (ALS)

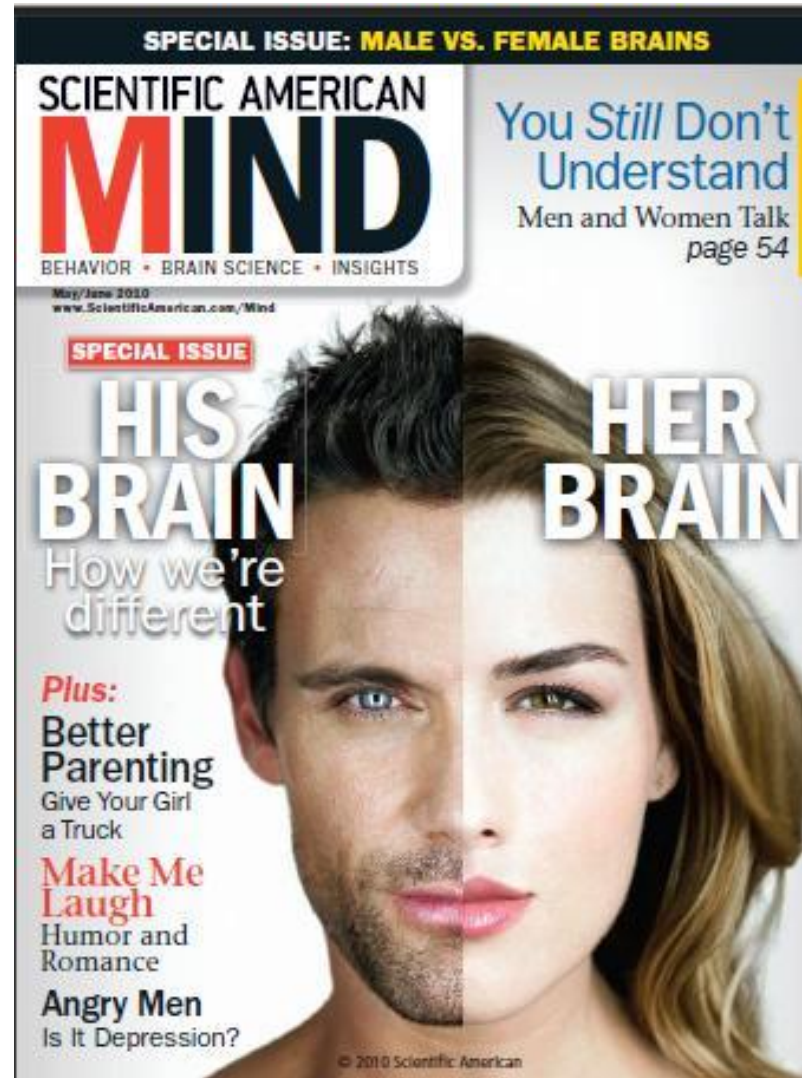
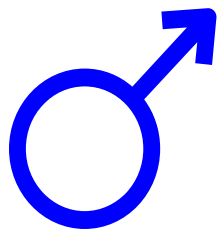
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Possible explanations

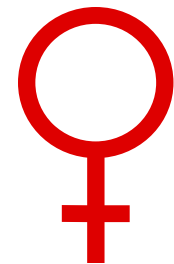
Felix, qui potuit rerum cognoscere causas
Happy the person who was able to know
the causes of things
(Virgil, 70-19 BC)

Brain differences in men and women

Men



Women



Scientific American MIND, May/June 2010

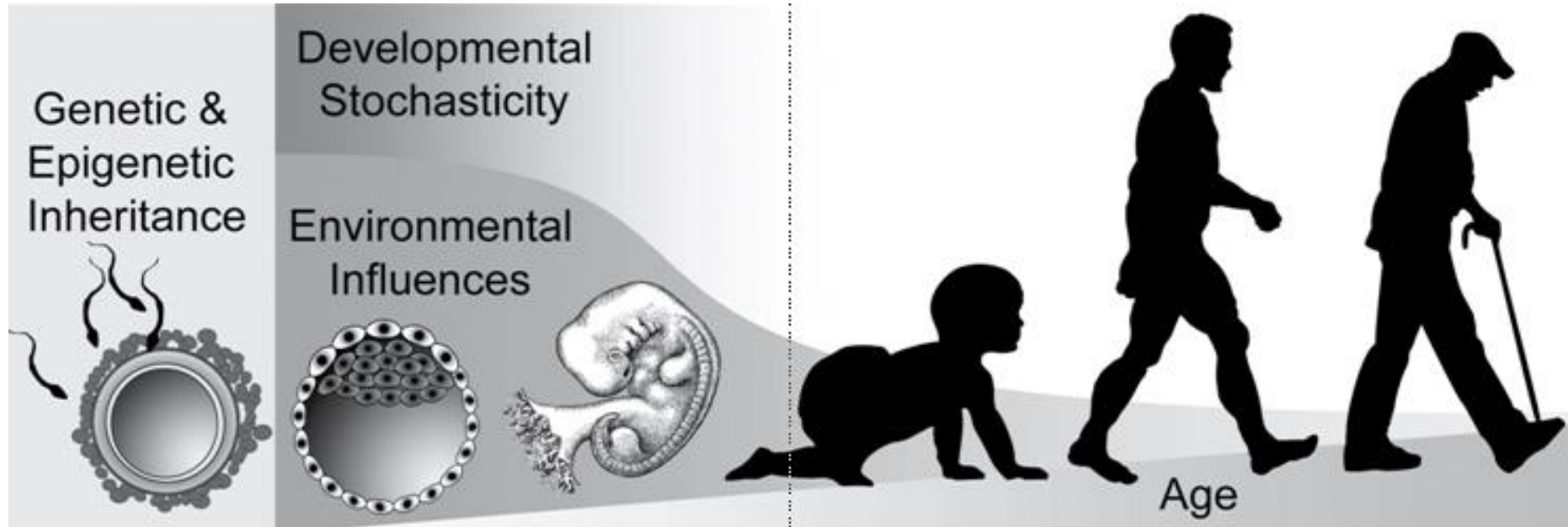
Sex = biology

- Chromosomes: XX vs. XY
- Gonads: ovaries vs. testicles
- Hormones: estrogen and progesterone vs. testosterone
- Reproduction: pregnancy, breast feeding, oral contraception

Gender = culture and society

- Subjective
 - Masculinity vs. femininity
 - Gender identity
- Societal and cultural (political)
 - Access to education
 - Access to jobs or sports
 - Access to medical care
 - Allowed to drive a car, vote for the president, or choose a partner

Life course approach

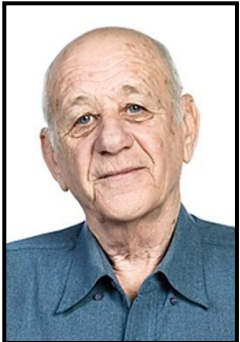


Protective factors -

Risk factors +

Dementia

Dimorphic life course approach



Protective factors -

Risk factors +



Dementia

Positive individual and societal changes

- Decline in heart disease and stroke incidence and mortality for 4-5 decades
- Better control of hypertension (e.g., β -blockers)
- Better control of diabetes (e.g., metformin)
- Better control of serum lipids (e.g., statins)
- Introduction of agents to prevent clots (e.g., low dose aspirin)

Changes in smoking, diet, and lifestyle

- Reduction in cigarette smoking – e.g., USA, from 1965 to 2009 (44 years).
 - Down from 52% to 24% in men
 - Down 34% to 18% in women
- Improved food preservation (refrigeration) and availability of fresh food long-distance
- Improved recognition of the benefits of exercise and physical activity (e.g., walking, swimming, yoga)
- Better information about prevention

Changes in education and socioeconomic factors

- Persons ≥ 65 years from 1990 to 2003 – USA
 - Up from 53% to 72% for high school diploma
 - Up from 11% to 17% for college degree
- Education and brain development and function (brain reserve), or better health behaviors
- Persons ≥ 65 years, median household net worth up from \$119,000 to \$196,000 from 1989 to 2005 – USA (in constant 2005\$)
- More wealth = better general living conditions (job, housing, heating + cooling, diet, medical care, etc.)

Changes in intelligence quotient (IQ)

- Mean IQ up 13.8 points in 46 years, 1932-1978 – USA
- Changes in environmental factors, education, and socioeconomic status
- Flynn effect. Remains partly unexplained

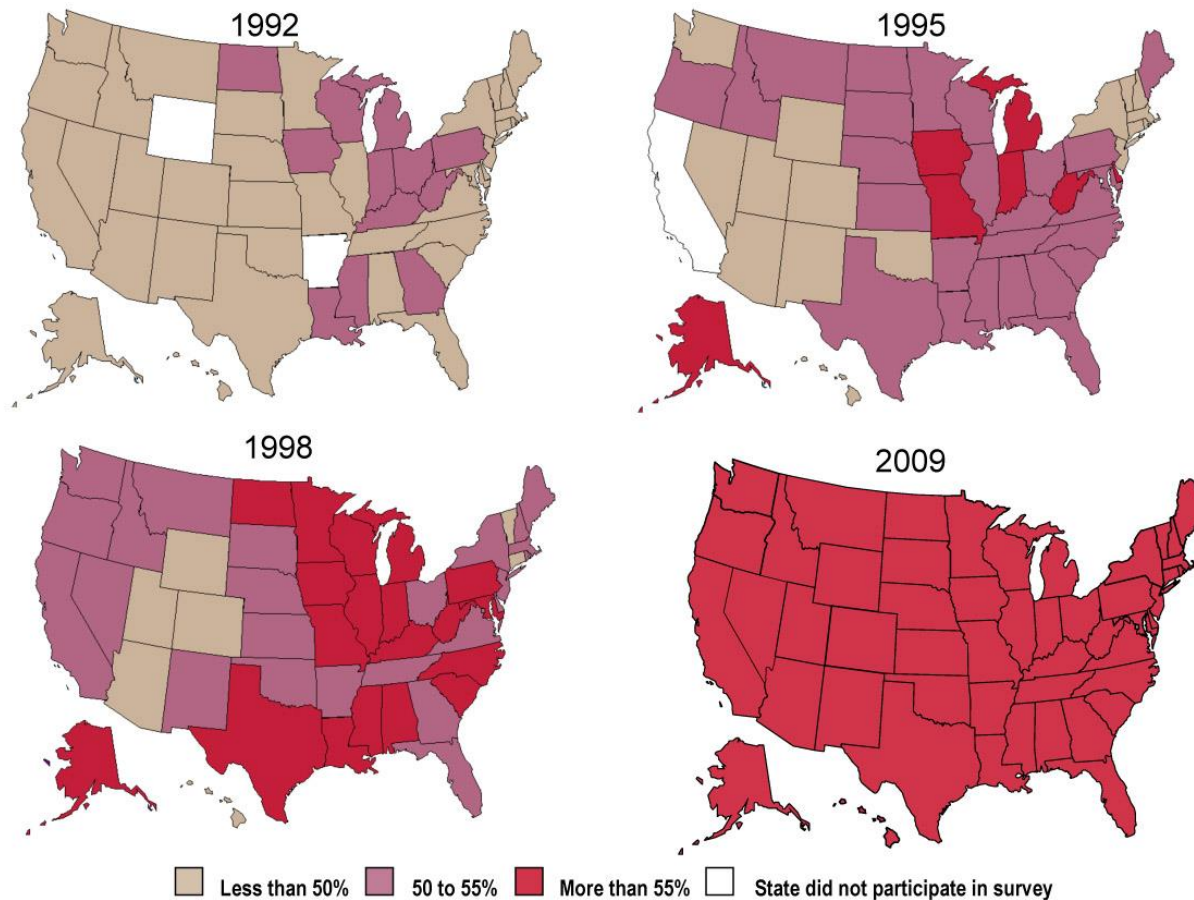
Negative individual and societal changes

- Improved survival after myocardial infarction and stroke
- Increased prevalence of subclinical vascular disease (silent strokes)
- Increased prevalence of hypertension and diabetes - e.g., US African Americans > 65 years, 1994-2002
 - Up from 73% to 83% for hypertension (+ 10%)
 - Up from 26% to 36% for diabetes (+ 10%)
- Increased prevalence of obesity
- Increase in multimorbidity and polypharmacy

The epidemic of obesity: 1992-2009

Trends in Overweight* Prevalence (%), Adults 18 and Older, US, 1992-2009

**Overweight
BMI ≥ 25**



*Body mass index of 25.0 kg/m² or greater. Source: Behavioral Risk Factor Surveillance System, CD-ROM (1984-1995, 1998) and Public Use Data Tape (2004-2009), National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 2010.

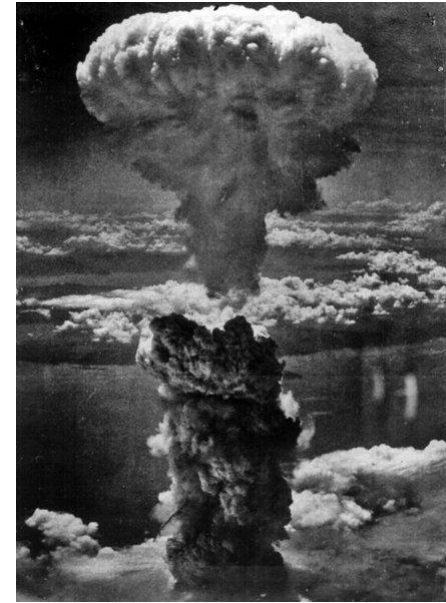
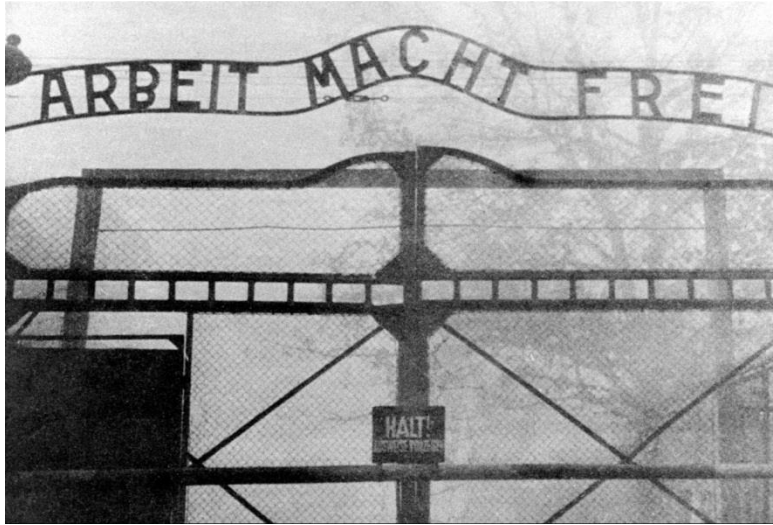
History

- The men and women who became demented in the past 20-30 years lived through more than half a century of history
- Positive events: electricity, telephone, radio, television, computers, internet, refrigeration and food transportation, airplanes ...
- Negative events: epidemics, natural disasters, climate changes, urbanization, pollution, wars, violence, traumas, famine, persecution, incarceration, migration, stress ...
- History affects men and women differently

Historical events

- 1914-1918: World War 1; Russian Revolution
- 1916-1920: Spanish flu pandemic
- 1929-1937: The Great Depression
- 1940-45: World War 2, concentration camps, atomic explosions, restriction of food, stress
- 1945-1989: Cold War, Korea War, Vietnam War
- 1960s: Student protests and terrorism in Europe
- 1989: End of the Eastern block and cold war
- Gulf War 1; September 11, 2001; Gulf War 2, and destabilization of the Middle East
- 2010-2011: The Arab spring

Historical events



3

Conclusions: hope for prevention

Truly I live in dark times!

(Bertolt Brecht, 1940)

Living in the end times

(Slavoj Zizek, 2010)

History and diseases

- The burden of disease is malleable, may change
- Humans can modify the burden of diseases
- Diseases appear and disappear in history over epochs (e.g., syphilis, tuberculosis, Zika, pellagra, peptic ulcer)
- The trends may vary by sex and gender, race/ethnicity, and across countries
- Trends of chronic disease reflect complex interactions; they are very delicate (ephemeral and contingent)
- Cautious optimism and pragmatic narratives
- Possible opposing trend for AD and other dementias

Prevention of dementia

- Modify risk factors in **the entire population**
 - May need to be very early in life
 - Environmental protection (air, water, food)
 - Better education, physical activity, cognitive stimulation
 - Focus prevention on **people at high risk**
 - Prediction score or formula
 - Genetic risk score (family history, *APOE* genotype)
-
- Early diagnosis and **secondary prevention**
 - Biomarkers, early manifestations, imaging, CSF
 - Neuroprotective drug or other intervention
 - **Treatment** after onset of AD or dementia

Conclusions

“History offers reasons for hope”

however,

“Rocca and colleagues have warned that increases in obesity, diabetes, and hypertension could undermine the gains achieved through improved education, wealth, and control of vascular risk factors.

Even if a dementia decline has begun, it might not last: the outcome depends on the balance of diverging trends.”

Thank you



*“The river flowed from century to century,
and human affairs play themselves out on its banks.
Play themselves out to be forgotten the next day, while the river flows on.”*
(Milan Kundera, 1984)